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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,687	09/28/2000	David Wallach	WALLACH=25	7238

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EXAMINER

LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 06/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/671;687

Applicant(s)

WALLACH ET AL.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/7/03.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-4, 20-24 and 38-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2, 4, 20-24 and 38-43 is/are rejected.
- 7) ☒ Claim(s) 3 and 44-46 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/646,403.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Receipt is acknowledged of two replies, filed April 4, 2003 and April 7, 2003 as Paper Nos. 12 and 13, to the previous Office Action. Amendments were made to the claims. Specifically, claim 1 was cancelled, and new claims 38-46 were added.

Claims 2-4, 20-24 and 38-46 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, Paper No. 11, mailed December 4, 2003, that is not addressed in this action has been withdrawn.

Because this action maintains rejections set forth in a previous Office Action and applies rejections to amended claims without raising new issues that are not necessitated by amendment, this Office Action is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4, 20-24 and 38-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons set forth in the previous Office Action, and is now applied to newly added claims 38-43 for the reasons set forth in the previous Office Action.**

Response to Arguments Regarding Claim Rejections - 35 USC § 112

Applicant's arguments filed April 4, 2003 have been fully considered but they are not persuasive. The following points are an accurate synopsis of applicant's arguments regarding the outstanding rejection:

1. Applicant contends that Example 14 of the Revised Interim Written Description Guidelines Training Materials is an accurate exemplification of the instant claims, and that the written description of the instant specification meets the standards as set forth in the specific example.

These standards can be further broken down into the following categories:

- A. That the variants of the claimed protein have a specified catalytic activity/function.
- B. That there be routine procedures for making the active/functional variants.
- C. That an assay be provided by which to test the catalytic activity of the claimed protein.

Applicant concludes that, based upon the purported satisfaction of the written description requirements set forth by this example, the single species described in the instant invention is representative of the genus that is claimed.

2. Applicant criticizes the examiner's rationale regarding the written description rejection as being hypothetical, wherein the examiner raises issues regarding the effects that any amino acid change might (original emphasis) have. Applicant's criticism includes the following statements:

- A. That it is much more common that random changes will have no effect on the relevant properties of the protein.

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- B. That many portions of a long protein have nothing whatsoever to do with the specific activity being claimed, therefore changing these portions would not be expected to affect functionality.
- C. That the examiner is attempting to unduly limit applicant to only the exemplified embodiment.
3. Applicant states that it would not require undue experimentation to determine whether or not a given analog binds TRAF2.
4. Applicant dictates that, with respect to Example 14, 95% identity is an arbitrary number, and that as little as 85% identity should meet the written description requirement in this particular case. No specific reason is given.
5. With regard to "fragments" of the claimed sequence, applicant indicates that truncating the sequence from the amino and carboxy terminus (individually or in combination, it is presumed) of the protein one amino acid at a time, and then measuring the function of the truncated protein in an assay, is well within the skill of the artisan. Furthermore, the skilled artisan would appreciate that when said functionality is no longer present, no further truncation is necessary.

The written description requirement is satisfied when the skilled artisan can envision the claimed embodiment of the invention by relying on either the prior art or the instant specification. Thus one must consider both the prior art and the instant specification when determining whether or not the written description requirement has been met. In the instant case, both the prior art and the instant specification have been considered with respect to the claimed genus of protein variants and fragments that bind to TRAF2, but the written description is found

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to be lacking. As it regards applicant's arguments, several issues have not been satisfied or addressed with regard to the rejection. For applicant's ease, these issues are addressed in a point-by-point manner relative to the arguments set forth above.

1. For the sake of argument, the examiner is willing to accept that Example 14 is an adequate representation of the instant claims. That being said, applicant contends that the instant specification describes "variants" of the claimed sequence in the same manner as set forth in Example 14, in that (A) a functional limitation, (B) a well established procedure for making "variants" having the functional limitation, and (C) a method for testing these variants is set forth in the disclosure. The examiner disagrees with applicant's interpretation for the following key issue: applicant has not described a procedure for making variants *which retain the functionality* of the claimed sequence.

In Example 14, specifically on page 53 of the Revised Interim Written Description Guidelines Training Materials, it is clearly stated that the procedures for making variants must retain the activity of the protein, in this case the ability to bind to TRAF2. In order to have procedures that result in the retention of this activity, the skilled artisan would need to know what portions of the claimed protein sequence were absolutely required for this activity. Applicant only provides *general* teachings for making additions, deletions, insertions or substitutions to a given protein sequence, and it is agreed that these teachings are routine in the art. However, applicant has not provided the requisite teachings of how to make *specific variants* of the claimed protein sequence that will *retain functionality*. This is because there are no teachings in either the prior art or the instant specification describing the portions of the claimed sequence that are required for binding to TRAF2. Without knowledge of the regions of

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the claimed protein sequence that are required for its ability to bind to TRAF2, the skilled artisan would not be able to predictably apply the general teachings provided by applicant for the purpose of making variants of the claimed protein sequence that retain the ability to bind to TRAF2. In other words, the skilled artisan cannot envision what variants can be made using the disclosed general teachings, wherein the variants comprise the required limitations of being 85%, 90%, 95%, etc., identical to the claimed sequence, as well as having the ability to bind TRAF2. Since the skilled artisan cannot envision these specific variants, the methods for making these specific variants cannot be routine, thus the written description requirement has not been satisfied with regard to Example 14.

The examiner would like to acknowledge that if the domains or particular features of the claimed sequence that were required for function were known in either the prior art or disclosed in the instant application, that the skilled artisan could envision making variants of the claimed sequence using the general teachings in the art. However, there is no such teaching on the record or in the Examiners own search for such information. Therefore, applicant has not conformed to the stated parameters set forth in Example 14, used in support of applicant's assertion of a satisfactory written description. As a result, this argument is insufficient to overcome the written description rejection.

2. Applicant's criticism of the examiner's rejection will be addressed in a point-by point fashion. However, the examiner would like to clarify that the hypothetical effects of a "variant" goes beyond a simple amino acid change, and includes the effects conveyed by all aspects of variations (e.g., deletions, insertions, substitutions and additions) set forth in the specification.

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A. While it may be true that random changes *may* not affect the function of a protein, the skilled artisan could not reasonably be apprised of what changes could be made with regard to any specific protein unless there was a description indicating what portions of the specific protein were absolutely necessary for its function. If the specification and the prior art do not describe where these changes can and cannot be made, it is impossible for the skilled artisan to be able to envision such changes. As such, the skilled artisan cannot routinely make variants of a protein when they have no idea of whether or not they are affecting the function of the protein. Rather, applicant's arguments appear to suggest that it is the skilled artisan's burden to uncover what the minimum TRAF2 binding regions are for the claimed sequence. This clearly cannot satisfy the written description requirement if someone other than applicant is required to do further experimentation to determine the nature of the invention.

B. Again, it may be true that many portions of a long protein have nothing whatsoever to do with the specific activity being claimed, therefore changing these portions would not be expected to affect functionality. However, the instant specification does not describe what portions of the claimed protein are absolutely required for the ability to bind TRAF2, and which portions can be changed without affecting the specific activity of the protein. Therefore the skilled artisan cannot envision what changes can and cannot be made to the claimed protein, while still retaining both the 85% identity and TRAF2 binding limitations set forth in the claim. Again, it appears that applicant is arguing that it is the skilled artisan's burden to uncover what the minimum TRAF2 binding regions are for the claimed sequence.

C. The examiner disagrees that an attempt is being made to unduly limit applicant to only the specific embodiment that is exemplified. It is simply a fact that applicant has not

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provided enough of a written description of the claimed protein such that the skilled artisan would be apprised of what variants were acceptable in terms of meeting the functional limitations of the claims. If the specification described what domains or pertinent sequences were absolutely required for meeting the functional limitations of the claims, there would be no written description issue regarding fragments or variants. This is because the skilled artisan would know to apply the general teachings regarding amino acid substitution, deletion, etc., to the specific portions of the protein that were irrelevant to the ability to bind TRAF2. However, the specification only describes one embodiment and some general teachings as it regards making protein variants, and expects the skilled artisan to hunt for functional variants by trial and error experimentation.

3. The applicant again disagrees that it would not require undue trial and error experimentation to determine if a variant could bind to TRAF2. According to the definition of variants in the specification, there are an unlimited number of variants that could be made for the claimed sequence. However, the skilled artisan could not reasonably predict which variants would meet the limitations of the claims, because there is no description in either the prior art or in the instant specification of what specific portions of the claimed sequence are required for binding to TRAF2. As such, the skilled artisan would be required to make changes to the sequence randomly, without any inkling of an idea as to whether or not the variant would have TRAF2 binding activity. The skilled artisan would then be required to practice unpredictable and undue trial and error experimentation to ascertain the true nature of the instant invention

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4. Applicant's argument that a protein with 85% identity to the claimed sequence would satisfy the written description requirement as sufficiently as a protein with 95% identity to the claimed sequence is arbitrary. There appears to be no support for this argument by precedent in the prior art or the instant specification. As such, the argument is moot.

5. Applicant's argument that it would be routine to truncate the claimed sequence one amino acid at a time from either the amino or carboxy terminus is again interpreted as an indirect admission that the instant specification does not describe functional variants of the claimed sequence. Rather, the argument indicates that it is the skilled artisan's burden to uncover functional variants and fragments of the claimed TRAF2 binding sequence by performing further unpredictable experimentation. However, the ability to perform further experimentation to determine if something meets the limitation of the claims, as it stands on its own, is not indicative of a written description of the claimed invention. Rather, the ability to make routine variants combined with the knowledge of where variations can be made without affecting the activity of a protein is required to satisfy the written description requirement. As such, applicant's argument is not found persuasive, thus the written description rejection is maintained.

In conclusion, the examiner would like to clarify the following points:

1. In order to satisfy the written description as set forth in Example 14 of the Revised Interim Written Description Guidelines Training Materials, either the prior art or the instant specification must provide a functional activity for the claimed sequence, a routine method of making functional variants for the claimed sequence which result in the retention of the functional activity, and a method of testing the variants for the functional activity. In the instant case;

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routine methods of making functional variants have not been disclosed because the skilled artisan would not be able to apply the general teachings for making variants to the specific protein in the absence of a description of where such variations could be made without affecting the function of the protein.

2. The description of what portions of the claimed TRAF2 binding sequence are required to bind to TRAF2 would be deemed to be descriptive of fragments or functional variants of the proteins having the functional activity. However, applicant has only described the ability of the full-length protein to bind to TRAF2, and gives no indication of what portions of the protein are required for this activity. This applicant is improperly seeking protection for an invention that is yet to be discovered (e.g., functional variants or fragments of the TRAF2 binding protein), simply by showing the invention can be discovered using general teachings in the art.

Applicant has simply provided a "road map" which could lead to the invention of fragments and variants of the claimed TRAF2 binding protein, and does not describe the actual fragments or variants in any detail. Therefore the written description rejection set forth previously is maintained.

Allowable Subject Matter

Claims 3 and 44-46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
June 23, 2003


DAVID GUZO
PRIMARY EXAMINER